



Toolbox

Secondary prevention of transient ischemic attack and stroke

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Stroke or transient ischemic attack is common and likely to be fatal or cause serious disability. A second stroke will not necessarily be of the same type as the initial event, although hemorrhages tend to recur (table 1). Patients with previous stroke commonly succumb to other vascular events, in particular myocardial infarction. Effective secondary prevention depends on giving attention to all modifiable risk factors for stroke and treating the causes of the initial stroke. Four questions should be answered:

IS IT ACUTE CEREBROVASCULAR DISEASE?

The key features of acute cerebrovascular disease are focal neurologic deficit, sudden onset, and the absence of an alternative ex-

Table 1 Risk of recurrence after stroke or transient ischemic attack

Event	Risk of stroke
Stroke	8% a year
Transient ischemic attack	8% in first month 5% a year thereafter 5% a year*

*Risk of myocardial infarction.

Modifiable risk factors for stroke

- Hypertension
- Smoking
- Diabetes mellitus
- Diet: high salt and fats, low potassium and vitamins
- Excess alcohol intake
- Morbid obesity
- Little physical exercise
- Low temperature
- Cholesterol concentration—at least in patients with coronary disease

Embotic causes of stroke found on echocardiography

- Mitral stenosis
- Left atrial enlargement (>4 cm)
- Dyskinetic or akinetic left ventricle
- Severe global left ventricular dysfunction
- Valvular vegetation
- Left atrial or ventricular thrombus
- Mitral valve calcification
- Calcific aortic valves or stenosis predispose to embolism but may not justify anticoagulation

planation. An abrupt onset of a dense hemiparesis before gradual improvement in a conscious patient rarely causes doubt, but conditions that commonly mimic stroke must be considered (see previous article in *West J Med* 2000;173:209-212).

IS IT ISCHEMIC OR HEMORRHAGIC STROKE?

Neither clinical history nor examination can reliably distinguish infarction from primary intracerebral hemorrhage. A small hemorrhage can produce transient symptoms, although these rarely resolve within an hour.

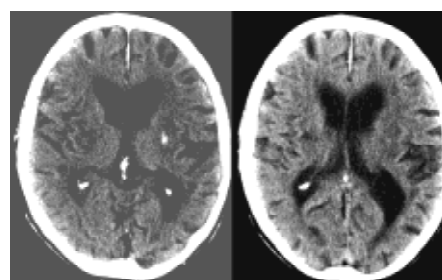


Figure 1 Computed tomograms on days 0 (left) and 8 (right) after left subcortical hemorrhage presenting as a transient ischemic attack with symptoms lasting 50 minutes. Note the resolution of diagnostic appearance at day 8.



Figure 2 (top) Magnetic resonance image (MRI) of posterior fossa of brain in patient with right cerebellar infarction. (bottom) A T1-weighted MRI of left subcortical hemorrhage (day 9 in patient in figure 1).

Cerebral imaging is essential, and the choice and timing of the scan are important (figure 1). Hemorrhage is immediately apparent on computed tomography, but its distinctive appearance becomes indistinguishable from infarction over a few weeks; for major symptoms, a computed tomogram

Table 2 Suggested imaging approaches for patients with symptoms of stroke

Symptoms	<1 hr*	Duration	
		1 hr; onset <2 wk	>1 hr; onset >2 wk
Abrupt onset, typical cerebrovascular symptoms	Image only if anticoagulation proposed	CT	MRI
Insidious onset, possibly tumor	NA	CT with contrast	CT with contrast
Insidious onset, suggests multiple sclerosis	NA	MRI	MRI

CT = computed tomography; MRI = magnetic resonance imaging; NA = not applicable.

*A shorter interval may be applied depending on available resources.

taken within 2 weeks should still be diagnostic (table 2), but a small hemorrhage may be missed after 1 week.

Magnetic resonance imaging has a greater sensitivity than computed tomography for brain stem, cerebellar, and small ischemic strokes of the brain. It can also identify hemorrhagic stroke and remains diagnostic long after signs have become undetectable on computed tomography (figure 2).

IS THE CAUSE CARDIOEMBOLIC OR VASCULAR?

As many as a quarter of ischemic strokes are caused by embolism from the heart or major vessels. In these patients, full anticoagulation should be considered. Embolic stroke can affect any vascular territory but can rarely

be diagnosed conclusively. Certain features should prompt a search for an embolic source. Transthoracic echocardiography is usually adequate, but transesophageal echocardiography is justified if the results are equivocal or the index of suspicion is high.

IS THE ANTERIOR OR THE POSTERIOR CIRCULATION INVOLVED?

The vertebrobasilar arteries supply the brain stem, cerebellum, and occipital lobes; the cerebral hemispheres are supplied through the carotid arteries. This distinction is important because carotid Doppler ultrasonography

with a view to endarterectomy is justified in patients with severe carotid disease only if symptoms have arisen from the anterior circulation (figure 3).

HOSPITAL REFERRAL

Although the approach to the investigation of stroke is simple, few general practitioners will have access to the necessary facilities or see enough cases to develop expertise in interpreting the results. Patients with possible stroke need urgent telephone or fax referral to a "fast track" specialist cerebrovascular clinic or stroke unit because of the time limitations on the diagnostic capability

Justifications for echocardiography

- Atrial fibrillation
- Heart failure
- Myocardial infarction within 3 months
- Electrocardiographic abnormalities: Myocardial infarction or ischemia Bundle branch block
- Cardiac murmur
- Peripheral embolism
- Clinical events in ≥ 2 areas: Right and left hemisphere Anterior and posterior circulation
- ≥ 2 cortical events (even in same area) unless severe ipsilateral carotid disease

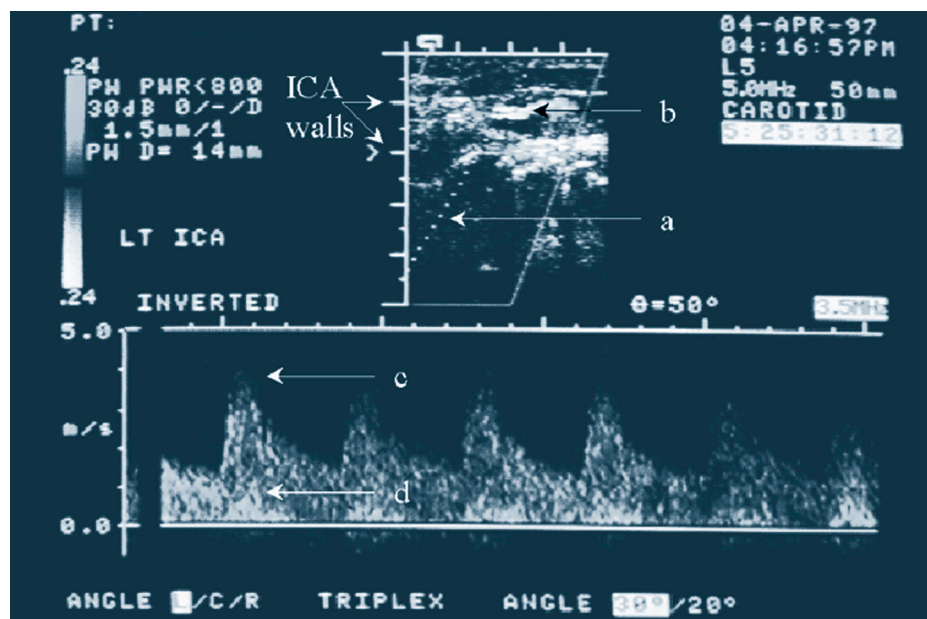


Figure 3 Carotid Doppler ultrasonogram in patient with severe internal carotid artery stenosis. The top panel shows the angle of insonation (a) of the internal carotid artery and sampling window (b); the velocity of systolic blood flow at the point of maximal narrowing (c) is nearly 4 m/s (normal <1 m/s). Stenosis causes flow velocity to increase and produces turbulence, which is seen as shading within the Doppler spectrum (d).

Table 3 Complex cases that may require hospital referral

Case	Possible treatment
Recurrent stroke or transient ischemic attack despite antiplatelet treatment (treatment failure)	Consider higher doses of aspirin, addition of dipyridamole (if not already prescribed), substitution or addition of clopidogrel, or substitution or addition of warfarin sodium
Recurrent embolic events despite adequate anticoagulation with warfarin	Consider adding low dose-aspirin
Recurrent nonhemodynamic symptoms from inoperable severe carotid stenosis or serious intracranial stenosis despite antiplatelet treatment	Consider warfarin
Hypertension and inoperable severe carotid stenosis	Consider cerebral blood flow monitoring (with ultrasonography or radionuclide perfusion scanning) before antihypertensive treatment

of computed tomography and the limited availability of magnetic resonance imaging (table 3).

MANAGEMENT OF RISK FACTORS

Smoking is an important correctable risk factor and should be strongly discouraged. The risk of stroke in a smoker returns to that of a nonsmoker within 3 to 5 years after stopping smoking.

The immediate reduction of blood pressure may be deleterious, but long-term risk is inversely related to the blood pressure achieved (table 4). Treatment may, therefore, be justified even in patients with "normal" blood pressures. Hypertension should be

treated 1 to 2 weeks after a stroke according to the British Hypertension Society guidelines (figure 4). Patients at high risk of a further stroke (such as elderly people) derive the greatest benefit from treatment.

The role of serum cholesterol concentration in the pathogenesis of stroke remains debatable. Nevertheless, HMG CoA reductase inhibitors (statins) have been shown to reduce the risk of stroke in clinical trials of patients with coronary artery disease. Lowering cholesterol concentrations with a statin after atherosclerotic stroke or transient ischemic attack probably reduces recurrent events and the risk of ischemic heart disease developing. Because stroke patients represent a high-risk group, the cost of treatment may be justified.

Diabetes confers a substantial disadvantage for survival and functional outcome on

patients with acute stroke. The mechanism for this is unknown, but because it is a long-term effect, attempts should be made to normalize blood glucose concentrations. Blood pressure targets are lower for diabetic than nondiabetic patients.

Elevated plasma homocysteine concentration is increasingly linked to premature vascular disease, and it can be easily lowered through vitamin supplements (folate and pyridoxine). Although the value of lowering homocysteine concentrations has not been proved, younger patients with raised plasma homocysteine concentrations may benefit from supplementation.

ANTIPLATELET THERAPY AND ANTICOAGULATION

Patients with atrial fibrillation should receive warfarin sodium if they have no contraindi-

Main contraindications to long-term warfarin sodium treatment

- Gastrointestinal bleeding
- Active peptic ulceration
- Frequent falls
- Alcohol misuse
- History of intracranial hemorrhage
- Age, by itself, is not a contraindication

Table 4 Blood pressure (BP) targets (mm Hg) in nondiabetic and diabetic stroke patients

BP target	No diabetes	Diabetes
Titrate to diastolic	≤85	≤80
Optimal	<140/85	<130/80
Suboptimal	≥150/90	≥140/85

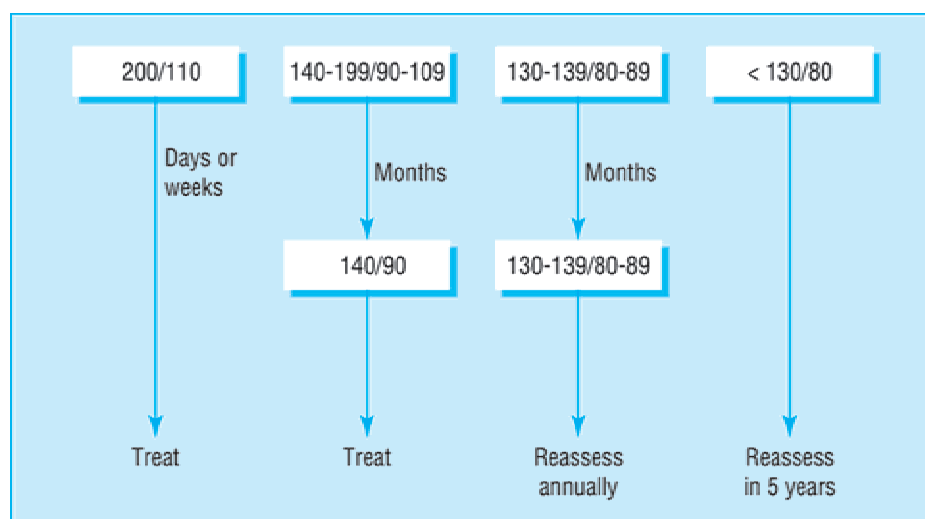


Figure 4 Blood pressure thresholds (mm Hg) for treatment after stroke or transient ischemic attack (based on British Hypertension Society guidelines 1999).

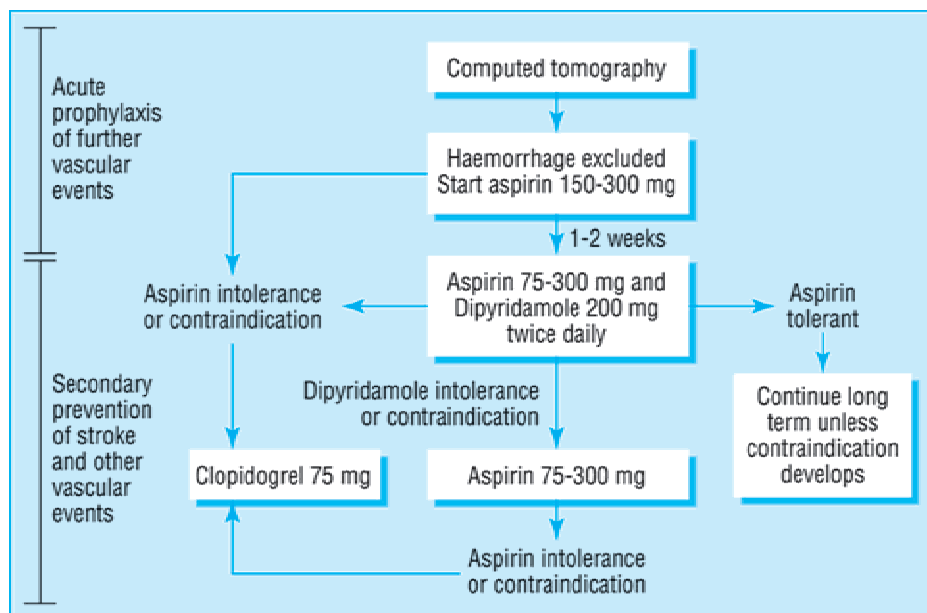


Figure 5 Aspirin as the first line of antiplatelet therapy after stroke

cations, aiming at an international normalized ratio of 2.0 to 3.0. Patients with other important sources of cardiac embolism also benefit from warfarin therapy. Only patients with mechanical prosthetic heart valves require a higher target international normalized ratio of 2.5 to 4.5, although the exact value depends on the type of valve.

For all other patients with ischemic stroke, antiplatelet therapy would be first-line treatment (figure 5). Aspirin is inexpensive and simple to administer, and its benefits are conclusively proved. An initial dose of 300 mg, followed by 75 mg daily, is advised (higher

doses have little advantage but increase gastrointestinal side effects and the incidence of bleeding).

Modified-release dipyridamole (200 mg twice a day) has an independent and additive effect to low-dose aspirin therapy in preventing further strokes but not coronary events or overall mortality. The routine addition of dipyridamole to the use of aspirin for secondary prevention of strokes may be cost-effective.

Clopidogrel (75 mg daily), a new antiplatelet drug, is well tolerated and was slightly more effective than aspirin in a large trial. However, it is not cost-effective for initial

Indications for carotid endarterectomy

Surgery not indicated

- Carotid area symptoms and ipsilateral stenosis of 0% to 69%
- Complete occlusion of the carotid artery

Surgery indicated

- Carotid area symptoms within 6 months and ipsilateral stenosis of 70% to 99%
- Carotid area symptoms within 12 months and ipsilateral stenosis of 80% to 99%

treatment. Clopidogrel should be used in patients with true intolerance to aspirin (allergy or intractable side effects with low-dose enteric-coated aspirin with or without the use of antiulcer drugs); dipyridamole alone does not prevent cardiac events.

CAROTID SURGERY AND ANGIOPLASTY

Firm evidence from 2 large trials has clarified the role of carotid endarterectomy in patients with ipsilateral severe carotid stenosis (figure 6). Patients with severe disease benefit from surgery for as long as 12 months after the most recent cerebral event. The benefit derived is inextricably linked to the operative risk (stroke or death within 30 days)(figure 7). In randomized trials, the operative mortality in patients with severe disease was



Figure 6 Angiogram showing tight stenosis of internal carotid artery just distal to the bifurcation

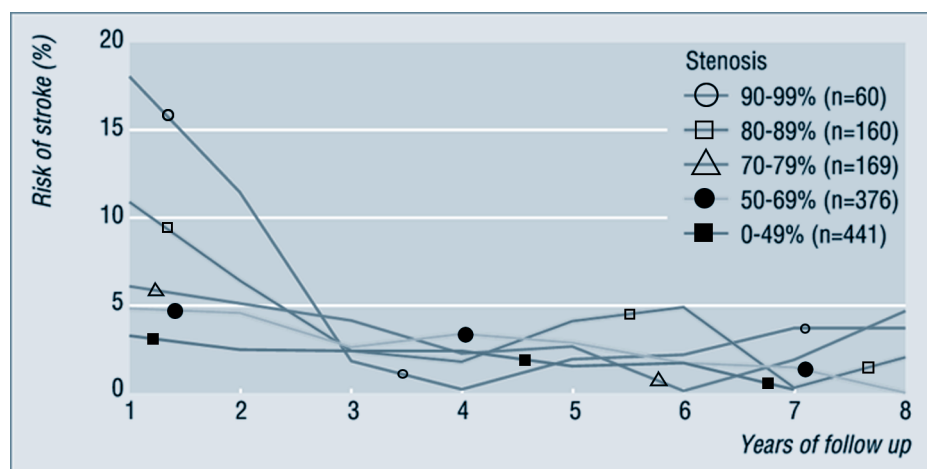


Figure 7 Risk of stroke in patients not having surgery according to degree of stenosis. Data from the European Carotid Surgery Trial (*Lancet* 1998;351:1379-1387).

Table 5 Summary of results from European Carotid Surgery Trial

Stenosis, %	Incidence of stroke, %		Absolute risk reduction, %	Relative risk reduction, %
	Surgery arm	Medical arm		
0-30	11.8	6.2	— 5.6 at 3 yr	None
31-69	16.0	15.0	— 1.0 at 5 yr	None
70-99	12.3	21.9	9.6 at 3 yr	44 at 3 yr

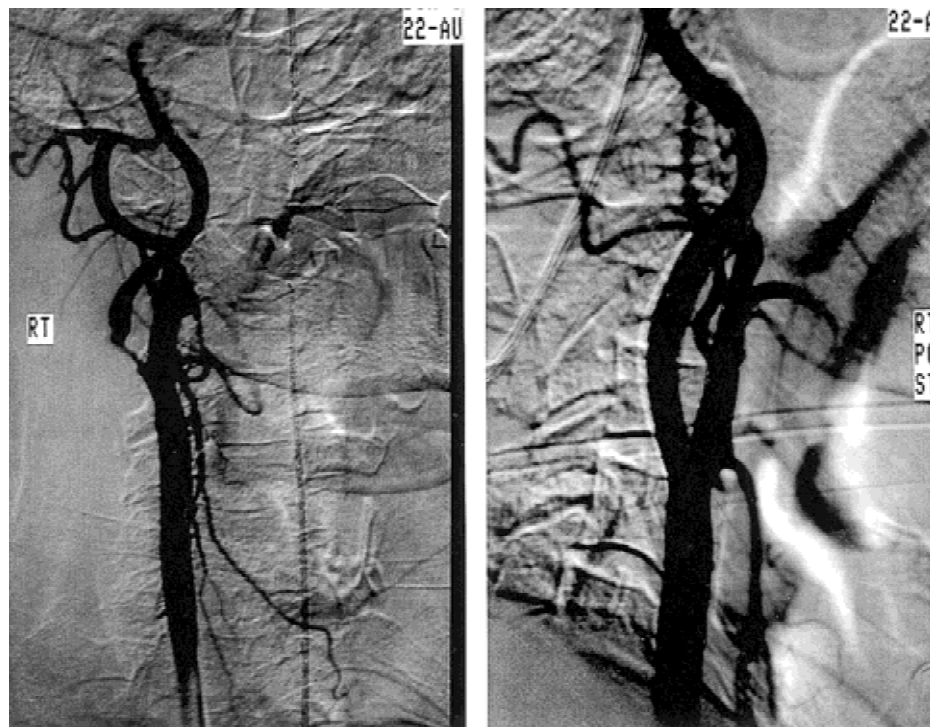


Figure 8 Severe carotid stenosis before (left) and after carotid angioplasty and stenting (right)

1.0%, the risk of death or disabling stroke less than 4.0%, and the risk of death or of any stroke less than 7.5% (table 5). Surgical risk is inversely proportional to surgical volume, implying that patients should be referred to busy carotid endarterectomy centers. Surgeons must quote their own risks rather than results obtained in trials.

Any patient presenting with carotid area symptoms should be considered a possible candidate for carotid endarterectomy, and carotid Doppler ultrasonography should be done if the patient is fit for surgery. The presence or absence of a carotid bruit is irrelevant. An ongoing meta-analysis may further refine the indications, particularly regarding the management of women and patients with

isolated retinal symptoms, who seem to have a lower overall risk of stroke.

A successful carotid endarterectomy is not a major procedure, and most patients can be discharged home the day after surgery. Neither clinical nor ultrasonographic surveillance prevents late stroke, and so most patients are discharged from follow-up at 6 weeks with the proviso that they should be referred immediately should further cerebral ischemic events occur.

In carotid angioplasty, the stenotic area is dilated by using a balloon catheter introduced percutaneously through the femoral artery (figure 8). The potential advantages of carotid angioplasty include reduced hospital stay and incidences of cranial nerve injury, wound

complications, and other cardiovascular morbidity. The main concern about carotid angioplasty is the risk of embolic stroke at the time of the procedure and recurrent stenosis. Carotid angioplasty aids the management of fibromuscular dysplasia, radiation injury, and symptomatic restenosis after carotid endarterectomy. Otherwise, carotid angioplasty should not be performed outside randomized trials, and as with carotid endarterectomy, outcomes in individual centers should be audited.

COMPLEX CASES

Secondary prevention of stroke is rightly the province of general practitioners, and the preceding suggestions concern most patients with recent stroke. However, patients with complex conditions need specialist services, although definitive trial evidence justifying therapeutic decisions in such patients is often absent. Patients should be monitored for compliance with treatment and the development of complications such as renovascular disease, ischemic heart disease, and further cerebrovascular problems. Optimal dietary, smoking, lipid, and blood pressure management is always required in addition to anti-thrombotic treatment.

G T McInnes and L Ramsay contributed toward the blood pressure guidelines. M R Walters supplied some of the pictures, and J Overell supplied the antiplatelet flow chart.

Further reading

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